Applicant: James Keck et al. Attorney's Docket No.: 21121-007US1/2307US **Preliminary Amendment**

Serial No.: 09/601,997

Filed : December 15, 2000

AMENDMENTS TO THE CLAIMS:

Please amend claims 58 and 59 as follows. This listing of claims replaces all prior such listings of claims.

LISTING OF CLAIMS:

Claims 1-8 (Cancelled)

- (Previously Presented) The method according to Claim 58, wherein said function is a physiological function.
- (Previously Presented) The method according to Claim 58, wherein said 10. function is enzyme activity.
- 11. (Previously Presented) The method according to Claim 58, wherein said function is protein synthesis.
- 12. (Previously Presented) The method according to Claim 58, wherein said function is expression of a biological factor.
- 13. (Previously Presented) The method according to Claim 58, wherein said function is a regulatory effector function.
- 14. (Previously Presented) The method according to Claim 58, wherein said phenotypic change is monitored directly.

Claims 15-57 (Cancelled)

- (Currently Amended) A high-throughput method of assigning a function associated with a product coded for by a sample nucleic acid sequence in a target nucleic acid molecule, said method comprising:
- a) without any intervening bacterial cloning steps and without any conformational modeling of mRNA transcribed from the target nucleic acid molecule that comprises the sample nucleic acid sequence, delivering into and amplifying and expressing a plurality of members of an oligonucleotide family as individual transcription products in a plurality of recombinant non-bacterial host cells comprising the target nucleic acid molecule that comprises the sample nucleic acid sequence, whereby the method is high-throughput, wherein:

each member of the oligonucleotide family comprises a plurality of nucleic acid molecules;

each member of the oligonucleotide family encodes a transcription product comprising a sequence that is complementary to a sequence contained in the mRNA

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transcribed from the target nucleic acid molecule that comprises the sample nucleic acid sequence;

the plurality of members of the oligonucleotide family are introduced into expression vectors, which are introduced into the host cells, wherein the expression vectors comprise: double-stranded DNA, comprising:

> a sense strand and an antisense strand, wherein the sense strand codes for an antisense strand that, when expressed as encodes RNA, that binds to an mRNA sequence transcribed from the sample nucleic acid in the target nucleic sequence so that expression of a product from the target nucleic acid is inhibited; and

means for determining directionality of expression, wherein the product is associated with at least one phenotypic property of a host cell containing the mRNA sequence; and wherein the expression vector is for expression in non-bacterial host cells;

the coding sequence for each individual transcription product encodes an antisense nucleic acid that binds to the mRNA transcribed from the target nucleic acid molecule that comprises the sample nucleic acid sequence; and

expression of one or more of the individual transcription products inhibits production of a product of the mRNA; and

- b) in the resulting host cells, comparing the phenotypes of the resulting host cells to phenotypes of control cells to identify analyzing changes in phenotype to thereby assign a function associated with the product encoded by the sample nucleic acid sequence in the target nucleic acid molecule, wherein control cells are untransfected host cells, whereby changes in phenotype can be assigned by comparison of the transfected host ceil, and the untransfected host cell.
- **59**. (Currently Amended) The method of claim 58, wherein the RNA that is produced from the sense strand of binds to an mRNA sequence transcribed from the sample nucleic acid in the target nucleic sequence so that expression of a product from the target nucleic acid is inhibited, comprises:

transcribed from the sample nucleic acid in the target nucleic sequence a catalytic domain that cleaves an the mRNA sequence transcribed from the sample nucleic acid in the target nucleic sequence; and

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> binding sequences flanking the catalytic domain for binding the RNA to the mRNA, and/or wherein the means for determining directionality of expression comprises a different non blunt-ended restriction enzyme site at each end of said double-stranded DNA.

60. (Original) The method of claim 59, wherein the double-stranded DNA is formed by contacting a first oligonucleotide with a complementary second oligonucleotide, and/or wherein the non blunt-ended restriction enzyme site is complementary to an end of the expression vector.

- 61. (Original) The method of claim 59, wherein said expression vector is formed by: (a) contacting a double-stranded oligonucleotide with an expression vector; or (b) by contacting a single-stranded oligonucleotide with said expression vector; or (c) contacting a triple-stranded oligonucleotide with an expression vector.
- 62. (Previously Presented) The method of claim 58, wherein the expression vector is a plasmid or a virus for expression in non-bacterial host cells.
- 63. (Original) The method of claim 62, wherein the virus is a retrovirus or an adeno-associated virus.
- 64. (Previously Presented) The method of claim 58, wherein the expression vector is transfected directly into mammalian cells.
- 65. (Previously Presented) The method of claim 58, wherein the sample nucleic acid is genomic DNA, cDNA, an expressed sequence tag (EST) or RNA.
- 66. (Previously Presented) The method of claim 58, wherein the family contains between 3 and 20 members.
- 67. (Previously Presented) The method of claim 58, wherein each member of the family is designed to inhibit the production of a product of the target nucleic acid molecule.
- 68. (Previously Presented) The method of claim 58, whereby all members of a family are assessed in a single experiment.
- 69. (Previously Presented) The method of claim 58, whereby a plurality of different target nucleic acid molecules and/or sample nucleotide sequences are assessed.
- 70. (Original) The method of claim 59, wherein the expression vector is a plasmid or a virus for expression in non-bacterial host cells.
- 71. (Original) The method of claim 60, wherein the expression vector is a plasmid or a virus for expression in non-bacterial host cells.

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(Original) The method of claim 61, wherein the expression vector is a plasmid 72. or a virus for expression in non-bacterial host cells.

(Previously Presented) The method of claim 58, wherein the oligonucleotide 73. family is a ribozyme family.

Claim 74 (Cancelled)